

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cohort Profile: A national, community-based prospective cohort study of SARS-CoV-2 pandemic outcomes in the U.S. - The CHASING COVID Cohort Study
<b>AUTHORS</b>	Robertson, McKaylee; Kulkarni, Sarah; Rane, Madhura; Kochhar, Shivani; Berry, Amanda; Chang, Mindy; Mirzayi, Chloe; You, William; Maroko, Andrew; Zimba, Rebecca; Westmoreland, Drew; Grov, Christian; Parcesepe, Angela; Waldron, Levi; Nash, Denis

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Chilimuri , Sridhar BronxCare Health System
<b>REVIEW RETURNED</b>	09-Feb-2021

<b>GENERAL COMMENTS</b>	<p>The authors present a comprehensive ongoing prospective cohort study investigating the determinants of SARS-CoV-2 infection in a large and diverse population across the US. The following are our recommendations.</p> <ul style="list-style-type: none"> <li>• Line 35 - 41. The reported number of cases and death appear to be discordant with CDC data. (<a href="https://covid.cdc.gov/covid-data-tracker/index.html#trends_totalandratedeaths">https://covid.cdc.gov/covid-data-tracker/index.html#trends_totalandratedeaths</a>)</li> <li>• Page 14, Line 12: we recommend that they elaborate the testing pattern preferences as described (e.g fast track, comprehensive, dual etc)</li> </ul>
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<b>REVIEWER</b>	Bazoukis, George Geniko Nosokomeio Athenon o Euangelismos
<b>REVIEW RETURNED</b>	28-Feb-2021

<b>GENERAL COMMENTS</b>	<p>Thank you for the opportunity to review this interesting study.</p> <p>I believe that provides important data during the current pandemic especially for the US population.</p> <p>It would be helpful to the reader if the authors modify the abstract section and especially the findings to date in order to provide a summary of the most interesting results of the study.</p> <p>Furthermore, i propose to re-write the conclusions section as in its current form it simply informs about the future plans, the aims of the study and its strengths.</p>
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<b>REVIEWER</b>	Murdoch, David University of Otago
<b>REVIEW RETURNED</b>	27-Mar-2021

<b>GENERAL COMMENTS</b>	<p>The paper describes a prospective cohort study looking at aspects of COVID-19, presumably established in haste early on the pandemic. The authors should be commended for the foresight to set up this study.</p> <p>Major comments:</p> <p>(1) The cohorts aims (stated as "objectives" on pages 6 and 7, but really are aims) are very broad. It would be helpful to also articulate more clearly the purpose of this paper, and this should be reflected in the title. Is the intention to give the initial description of the cohort? There will be many analyses and substudies in a cohort of this size, so being really clear and focused about the purpose of each paper will greatly help the reader. The paper should then retain this focus. The current paper only addresses some of the stated aims.</p> <p>(2) My main concern about this study is the generalisability of the findings. This is touched on by the authors, but there needs to be much more discussion about this limitation, including speculation about the impact of some obvious recruitment/selection biases. Recruitment mainly through social media will inherently mean that many groups will be under-represented in the study population. There is much more than just the impact of age. The COVID-19 pandemic has highlighted many inequity issues, and this needs to be discussed up front. There should also be a comparison of the study population demographics with the US population demographics in the effort to better characterise some of the concerns about generalisability.</p> <p>(3) The importance and particular advantages of this cohort over other datasets need to be clearly presented.</p> <p>Other comments:</p> <p>(1) The structure of the paper is a little unusual, with some sections seemingly in the wrong section. For example, there are findings in the section "Cohort eligibility" in the methods section. "Future plans" are included in the results section, when this would be better placed in the discussion.</p> <p>(2) The "Findings" section of the abstract needs to have more concrete findings of the study.</p> <p>(3) The value of the statistical analysis (Chi square, p-values) in Table 2 uncertain and could be omitted.</p> <p>(4) There should be more comparisons with other similar data from the US in the discussion section.</p>
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## VERSION 1 – AUTHOR RESPONSE

### Reviewer Reports:

Reviewer: 1

Dr. Sridhar Chilimuri , BronxCare Health System

Comments to the Author:

The authors present a comprehensive ongoing prospective cohort study investigating the determinants of SARS-CoV-2 infection in a large and diverse population across the US. The following are our recommendations.

- Line 35 - 41. The reported number of cases and death appear to be discordant with CDC data. ([https://covid.cdc.gov/covid-data-tracker/index.html#trends\\_totalandratedeaths](https://covid.cdc.gov/covid-data-tracker/index.html#trends_totalandratedeaths))

**Response:** We have reviewed the latest US data and have updated the number of cases and deaths in our manuscript accordingly.

- Page 14, Line 12: we recommend that they elaborate the testing pattern preferences as described (e.g fast track, comprehensive, dual etc)

**Response:** We have included quite a bit of detail on these analyses in the cohort profile and have referred readers who may be interested in more details to the publications. Given space constraints, we have not added more detail on these papers.

Reviewer: 2

Dr. George Bazoukis, Geniko Nosokomeio Athenon o Euangelismos

Comments to the Author:

Thank you for the opportunity to review this interesting study.

I believe that provides important data during the current pandemic especially for the US population.

It would be helpful to the reader if the authors modify the abstract section and especially the findings to date in order to provide a summary of the most interesting results of the study.

**Response:** We were following the guidelines of the journal for cohort profiles, and have not modified the abstract in response to this comment.

Furthermore, i propose to re-write the conclusions section as in its current form it simply informs about the future plans, the aims of the study and its strengths.

**Response:** Since it is a cohort profile paper and not a results paper per se, rather than recapitulate conclusions based on results of other analyses published elsewhere, we felt it was appropriate to conclude the Cohort Profile in this way that alludes to the potential results that the cohort could provide. However, we have deleted the conclusion section and replaced it with the overlapping section on Future Plans.

Reviewer: 3

Dr. David Murdoch, University of Otago

Comments to the Author:

The paper describes a prospective cohort study looking at aspects of COVID-19, presumably established in haste early on the pandemic. The authors should be commended for the foresight to set up this study.

Major comments:

(1) The cohorts aims (stated as "objectives" on pages 6 and 7, but really are aims) are very broad. It would be helpful to also articulate more clearly the purpose of this paper, and this should be reflected in the title. Is the intention to give the initial description of the cohort? There will be many analyses and substudies in a cohort of this size, so being really clear and focused about the purpose of each paper will greatly help the reader. The paper should then retain this focus. The current paper only addresses some of the stated aims.

**Response:** The intent is to give the description of the cohort study. The reviewer is correct that we have stated the broad aims of the larger cohort study, all of which cannot be addressed in this manuscript. In response, we have added a statement on the objective of the paper as follows:

*"The purpose of this cohort profile paper is to describe the origin of the cohort, the study design, and enrollment characteristics of the sample. We also present a sample of findings from the cohort to date."*

(2) My main concern about this study is the generalisability of the findings. This is touched on by the authors, but there needs to be much more discussion about this limitation, including speculation about the impact of some obvious recruitment/selection biases. Recruitment mainly through social media will inherently mean that many groups will be under-represented in the study population. There is much more than just the impact of age. The COVID-19 pandemic has highlighted many inequity issues, and this needs to be discussed up front. There should also be a comparison of the study population demographics with the US population demographics in the effort to better characterise some of the concerns about generalisability.

**Response:** While we agree with the reviewer that the cohort is not representative of the U.S. population, we disagree with the reviewer regarding the generalizability of our findings, particularly causal associations. Indeed, no longitudinal cohort studies are representative of any population. The same can be said of randomized trials. These study populations reflect myriad factors, including eligibility and exclusion criteria, self-selection factors, sources of participant recruitment, to name just a few. However, we rarely would say that the results of a vaccine trial (such as the COVID-19 vaccine trials) where participants were not reflective of the general population, are not relevant or generalizable to a larger population.

We have pointed out that our cohort is not representative, because we want to be clear that point estimates (e.g., prevalence or incidence of SARS-CoV-2) are specific to our cohort and are not 'national estimates'. We feel we have been very clear about this. But for reasons stated above, we do not feel it is appropriate to emphasize that findings from our cohort are not generalizable simply because our cohort population is not representative of the US adult population, nor is it part of our objectives to provide representative estimates. Moreover, for these same reasons, we do not include a comparison of our cohort demographics to that of the U.S.

(3) The importance and particular advantages of this cohort over other datasets need to be clearly presented.

**Response:** We agree, and have tried to emphasize this throughout in the revised submission. Please see, for example, the revised second paragraph in discussion.

Other comments:

(1) The structure of the paper is a little unusual, with some sections seemingly in the wrong section. For example, there are findings in the section "Cohort eligibility" in the methods section. "Future plans" are included in the results section, when this would be better placed in the discussion.

**Response:** Thank you for this point. We have replaced the conclusions section in the discussion with the section on Future Plans.

(2) The "Findings" section of the abstract needs to have more concrete findings of the study.

**Response:** We have added some more detail to the Findings section of the abstract.

(3) The value of the statistical analysis (Chi square, p-values) in Table 2 uncertain and could be omitted.

**Response:** We have omitted these statistical tests.

(4) There should be more comparisons with other similar data from the US in the discussion section.

**Response:** The main reason for this is that there are really no other similar studies. We have added the following language to the discussion in response to this issue raised by Reviewer 3:

*“While SARS-CoV-2 is understood to be transmitted from person-to-person via respiratory droplets and exhaled aerosols, the incidence of SARS-CoV-2 infection and risk factors for incident infection have not been well-characterized by routine case-based surveillance of SARS-CoV-2 diagnoses or by cross-sectional seroprevalence studies to date.<sup>1–3</sup> Globally, few prospective epidemiologic studies of SARS-CoV-2 have been published. One recent global systematic review of observational studies of SARS-CoV-2 that employed serologic or PCR testing found only 18 prospective studies.<sup>4</sup> Most were focused on healthcare workers or other occupational groups, individuals in congregate settings, evacuees, or cruise ships; none were community-based (i.e., focused on risk factors in communities vs other higher risk populations/settings).<sup>4</sup> A greater understanding of SARS-CoV-2 incidence and risk factors, and other pandemic-related outcomes, in community samples can substantially complement routine case-based surveillance of new SARS-CoV-2 diagnoses and cross-sectional serosurveys, serving to inform aspects of implementation of the public health response and policies.”*

1. Angulo FJ, Finelli L, Swerdlow DL. Estimation of US SARS-CoV-2 Infections, Symptomatic Infections, Hospitalizations, and Deaths Using Seroprevalence Surveys. JAMA Netw Open 2021;4(1):e2033706.
2. Bajema KL, Wiegand RE, Cuffe K, et al. Estimated SARS-CoV-2 Seroprevalence in the US as of September 2020. JAMA Intern Med [Internet] 2020;Available from: <http://dx.doi.org/10.1001/jamainternmed.2020.7976>
3. CDC. COVID Data Tracker [Internet]. 2020 [cited 2021 Jan 31];Available from: <https://covid.cdc.gov/covid-data-tracker/>
4. Oran DP, Topol EJ. The Proportion of SARS-CoV-2 Infections That Are Asymptomatic : A Systematic Review. Ann Intern Med [Internet] 2021;Available from: <http://dx.doi.org/10.7326/M20-6976>